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APPROPRIATION/BUDGET ACTIVITY RDT&E, Defense-wide BA2 Applied Research			R-1 ITEM NOMENCLATURE Biological Warfare Defense PE 0602383E					
COST (In Millions)	FY 2006	FY 2007	FY 2008	FY 2009	FY 2010	FY 2011	FY 2012	FY 2013
Total Program Element (PE) Cost	132.814	112.814	99.137	106.982	110.914	110.414	110.414	110.414
Biological Warfare Defense Program BW-01	132.814	112.814	99.137	106.982	110.914	110.414	110.414	110.414

(U) Mission Description:

(U) DARPA's Biological Warfare Defense project is budgeted in the Applied Research Budget Activity because its focus is on the underlying technologies associated with pathogen detection, prevention, treatment and remediation. This project funds programs supporting revolutionary new approaches to biological warfare (BW) defense and is synergistic with efforts of other government organizations.

(U) Efforts to counter the BW threat include countermeasures to stop pathophysiologic consequences of biological or chemical attack, host immune response enhancers, medical diagnostics for the most virulent pathogens and their molecular mechanisms, tactical and strategic biological and chemical sensors, advanced decontamination and neutralization techniques, and integrated defensive systems. This program also includes development of a unique set of platform technologies that will dramatically decrease the timeline from military threat detection to countermeasure availability.

(U) Program Accomplishments/Planned Programs:

	FY 2006	FY 2007	FY 2008	FY 2009
Unconventional Therapeutics	37.202	35.000	30.000	37.864

(U) This thrust is developing unique and unconventional approaches to ensure that soldiers are protected against a wide variety of naturally occurring, indigenous or engineered threats. Past successes in this effort have come from developing therapeutics that are designed to work against broad classes of pathogens. This has led to several significant transitions, a separate thrust in Anthrax countermeasures, and most recently a program at Defense Threat Reduction Agency (DTRA) that directly capitalizes on previous DARPA investments. Work in this area has also

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uncovered new approaches to therapeutics that, rather than attacking specific pathogens, enhance innate human immune mechanisms against broad classes of pathogens. Not only will these approaches be more effective against known pathogens, they also promise to offer substantial protection against unknown pathogens including engineered pathogens and emerging pathogens from third-world environments. An emphasis is on the discovery and development of technologies that will allow a rapid response (within weeks) to unanticipated threats, whether they are naturally encountered emerging diseases or agents from intentional attack. A variety of approaches will be developed to accelerate the capability to rapidly produce needed therapeutics for our warfighters in weeks rather than years. This program has a goal of radically transforming the protein design process by researching and developing new mathematical and biochemical approaches to the in silico design of proteins with specific functions. By determining the structure of a specific protein that binds with a specific pathogen, the manufacturing process for therapeutics will be greatly reduced. This program is also developing an interactive and functional in vitro human immune system using tissue engineering. This "immune system" will be able to test the efficacy of vaccines against threat agents that, at the present time, can only be tested in animal models, thus significantly decreasing the time needed and increasing the probability of success for biological warfare vaccine development. An additional focus is the development of entirely new technologies that will allow the rapid, cost-effective manufacture of complex therapeutic proteins such as monoclonal antibodies and vaccine antigens.

(U) Program Plans:

- Developed in vitro fabrication of three-dimensional tissue constructs, bioscaffolds and bioreactors.
- Develop technologies for nano-imprinting viruses that racapitulate the antigenic structures of the native virus.
- Develop approaches for on-site battlefield synthesis of small molecule therapeutics, including antibiotics.
- Develop technologies to allow rapid, inexpensive assessment of radiation exposure in humans.
- Develop and demonstrate an integrated in-vitro immune system that will emulate the human immune response in order to provide a means of evaluating new BW vaccines and therapeutics.
- Demonstrate the ability to predict known vaccine immunogenicity in humans solely by testing in the artificial immune system.
- Develop and validate new in vitro systems to predict toxicology of vaccines and immune modifiers.
- Develop a technical framework for the synthesis of millions of doses of a protein therapeutic within 12 weeks.
- Develop new approaches for rapid, high-yield synthesis of therapeutic proteins in bacteria, fungi, and yeast.
- Develop new methods for purification of therapeutic proteins from high-yield fermenters.
- Develop new approaches for assuring correct folding and mammalian post-translational modification of proteins by bacteria and fungi.

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	FY 2006	FY 2007	FY 2008	FY 2009
External Protection	15.500	16.542	15.137	18.118

(U) This program is developing and demonstrating a variety of external protection technologies to protect soldiers from the hazards of chemical, biological and radiological attack and other hazards such as large unstable weapons stores. The program includes the autonomous detection and self-cleaning of surfaces contaminated by an attack, and the safe neutralization of hazardous materials.

(U) Program Plans:
- Developed and demonstrated new approaches for decontamination of sensitive electronics.
- Develop and demonstrate active coatings that can be applied to surfaces to provide protection against chem-bio attacks.
- Develop and demonstrate a portable system to safely destroy chemical and biological warfare (CBW) stockpiles.
- Develop and demonstrate a microbial based demilitarization of such hazardous materials as explosives stockpiles.

	FY 2006	FY 2007	FY 2008	FY 2009
Advanced Diagnostics	7.854	12.572	14.000	19.000

(U) In the early stages, many illnesses caused by biological warfare (BW) agents have flu-like symptoms and are indistinguishable from non-BW related diseases. Early diagnosis is key to providing effective therapy. The advanced diagnostics program will develop the capability to detect the presence of infection by biological threat agents, differentiate them from other pathogens (including those of non-BW origin), and identify the pathogen even in the absence of recognizable clinical signs and symptoms (i.e., while the pathogen numbers are still low). Novel approaches including the use of breath and advanced mathematical analysis will be examined.

(U) Program Plans:
- Develop hyperspectral approaches for presymptomatic diagnosis of exposure to pathogens or other medical issues (including naturally occurring disease) that affect soldier health and performance.

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- Validate the presence of explosive volatiles in breath in the presence of a number of confounder variables.
- Adapt biosensors for breath-based diagnostics.
- Evaluate and demonstrate multiplexed pathogen detection in microliter samples.
- Demonstrate the capability to mechanically and reversibly alter a protein structure so as to alter the sensitivity and specificity of analyte detection.
- Develop new mathematical and diagnostic approaches to interpret biosignature data from individuals to determine if there will be a change in physiological status from health to disease and vice versa. Use these data to identify the kind of disease and need for treatment.

	FY 2006	FY 2007	FY 2008	FY 2009
Sensors	41.706	30.000	25.000	25.000

(U) The Sensors program goal is to develop a unique set of biological warfare (BW) sensors that will greatly improve sensitivity and response time to bacteria, viruses and/or toxins.

(U) The overall goal of DARPA's Handheld Isothermal Silver Standard Sensor (HISSS) program is to develop a sensor that is capable of detecting the entire biological warfare threat spectrum (bacteria, DNA viruses, RNA viruses and protein toxins) with the same "silver standard" specificity as current laboratory techniques, but in a fast, reliable, handheld unit. Today, this standard is achieved for DNA and RNA threats using polymerase chain reaction, which is slow because of the associated temperature cycling. For proteins, the standard is met using Enzyme Linked Immunosorbent Assay (ELISA), which requires skilled laboratory technicians to complete. The equipment required for these tests is bulky and difficult to use under field conditions. Under HISSS, DARPA will develop fundamentally new ways to exploit previously developed identification mechanisms (DNA and RNA primers, protein antibodies) in an integrated, isothermal system that will allow a single, handheld sensor to detect the full range of BW threats.

(U) The Spectral Sensing of Bio-Aerosols (SSBA) program involves the active probing of bioaerosols with electromagnetic (EM) energy, which holds the promise of extremely fast, and potentially long-range, detection and identification of bio agents. Only a small portion of the EM spectrum is exploited in today's trigger sensors (e.g., optically based particle sizers, sometimes enhanced with fluorescence measurements).

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However, anecdotal evidence suggests that other portions of the spectrum may offer substantial improvement in trigger sensors, as well as potentially agent-specific discrimination capability. Various types of spectra in the visible, infrared, and ultraviolet (UV) wavelengths are being measured for prototype systems development. Additional spectral information such as UV fluorescence lifetime and single particle mass spectroscopy is also being evaluated. DARPA is investing in these approaches, beginning with cross-spectrum data collection and performance models, followed by prototype sensor development. An aerosol testbed has been developed to provide calibrated exposures of threat agent simulants and complex clutter mixtures for sensor performance evaluation.

(U) Program Plans:

- Spectral Sensing of Bio-Aerosols
  - -- Downselected to most promising concepts.
  - -- Designed, built, and tested prototype sensor systems.
  - -- Evaluated the use of mass spectrometry for single particle identification and evaluated the use of multi-spectral fluorescence for stimulant identification in bulk.
  - -- Characterize sensor prototype behavior in operational environments against live bio-agent aerosols.
  - -- Characterize other prototype behavior in operational environments against agents.

- Handheld Isothermal Silver Standard Sensor
  - -- Designed a prototype HISSS device.
  - -- Developing stabilized reagents for fieldability.
  - -- Build prototype HISSS device.
  - -- Characterize HISSS prototype in laboratory and operational environments.
  - -- Test HISSS prototype against live threat agents.

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	FY 2006	FY 2007	FY 2008	FY 2009
Threat Agent Cloud Tactical Intercept Countermeasure (TACTIC)	12.500	10.000	10.000	4.000

(U) The TACTIC program will develop and demonstrate the capability to (1) rapidly detect, discriminate and identify an airborne chemical warfare agent/biological warfare agent (CWA/BWA) battlefield threat at stand-off distances, and (2) use countermeasures to neutralize and/or precipitate the threat before it reaches the targeted troops. This program will investigate identification methodologies including: bead-based assays for biological molecules, fluorescent assays for chemicals, retro-reflector assays for chemical and biological agents; all of which can be interrogated with stand-off optical detectors. To accomplish the removal of the threat, technologies that mimic the seeding of rain clouds will be developed for particulate bio-agents, and technologies that react with chemical agent vapor will be investigated. Upon successful demonstration of the identification and removal technologies, a system will be developed to demonstrate the removal of chemical and biological simulant clouds from the battlefield.

(U) Program Plans:

- Investigated technologies for CWA/BWA standoff assays that rapidly (within one minute) identify agents.
- Investigated technologies to remove the agent cloud so as to eliminate the threat to unprotected war-fighters.
- Tested detection assays and cloud removal technologies in large scale test chambers. Validated levels of detection and elimination that will enable an effective TACTIC system.
- Developed models of identification and removal technologies. Carried out systems trades between competing identification and removal technologies.
- Integrate optimal identification and removal components into a prototype system.
- Test prototype system in scaled aerosol test chambers.
- Demonstrate system in full-scale field trials.
- Transition to Joint Program Executive Office - Chem Bio Defense (JPEO-CBD).

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	FY 2006	FY 2007	FY 2008	FY 2009
Mission-Adaptable Chemical Sensors (MACS)	10.652	7.700	5.000	3.000

(U) At present, chemical sensors are unable to combine sensitivity (parts-per-trillion) and selectivity (unambiguous identification of molecular species) with low false alarm rate. This effort will develop a sensor, based upon rotational spectroscopy of gases that will have superior capability in all categories; it will achieve the highest possible sensitivity (parts-per-trillion) for unambiguous detection of all chemical species. A preliminary blind test showed complete and unambiguous identification with a sampling time of one second and a false alarm probability below 0.001%. At present, the program has investigated the nature of the atmospheric background "clutter" at the parts per billion (ppb) level and below to enable the identification of target signatures at highest sensitivity. The program will focus on reduction of size and simplicity of function to achieve portability and simultaneous detection of a large number (hundreds) of species. The capabilities will far surpass all other current sensors.

(U) Program Plans:

- Design and build a portable form factor, high-sensitivity chemical sensor system and demonstrate its performance in a high-clutter atmospheric background.
- Demonstrate fractionation and related improvements to the system for improved simultaneous identification of multiple species in seconds.
- Refine initial form factor design and build a compact, fully portable, high-sensitivity sensor system.

	FY 2006	FY 2007	FY 2008	FY 2009
Immune Buildings (IB)	2.500	0.000	0.000	0.000

(U) DARPA has developed technologies for integrated defensive systems to be employed in military buildings to protect and respond to the emerging threat of aerosolized Chemical, Biological and Radiological (CBR) releases. The approach was to modify and augment the infrastructure of buildings to allow them to sense and defeat an attack by biological or chemical agents in real-time and to find and remove hazardous radiation left behind by a "dirty bomb." The program's emphasis areas were: to protect the human inhabitants from the effects of the agents; to restore the building to function quickly after the attack; and to preserve forensic evidence for treatment of victims, and for attribution.

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For CB releases, the DARPA focus was on the challenging problem of protection from internal releases of agent, where active and timely control of airflow is required to prevent a building's HVAC system from spreading the agent throughout the building. To enable such building-protection systems, DARPA developed component technologies such as optimized filtration systems, advanced neutralization techniques, and remediation techniques appropriate to biological, chemical, and radiological decontamination. These systems have transitioned for military use via a full-scale demonstration of a complete building protection system. In addition, a software tool was developed that demonstrates the design and optimization of building-protection systems for other military facilities.

(U) Program Plans:
- Continued development of neutralization technologies and reduced-false-alarm CW and BW sensors.
- Characterized the demonstration site facility and developed a prototype active protection system optimized for that site.
- Validated toolkit predictions in full-scale test beds and at demonstration site.
- Extended the software toolkit to provide cost analysis of protective system and further validate with performance and cost data from the demonstration site.
- Developed technologies to hyper-accelerate description of radioactive contamination within building materials and to rapidly mobilize the contamination of outer building surfaces for more efficient removal.
- Installed complete IB protective system in an active military facility at Ft. Leonard Wood, MO.
- Transitioned IB systems to the U.S. Army Chemical School and U.S. Army Corps of Engineers.

	FY 2006	FY 2007	FY 2008	FY 2009
Asymmetrical Products for BWD	1.300	0.000	0.000	0.000

(U) Program Plans:
- Continued to develop a technical approach to induce mucosal immunity against BioWarfare (BW) pathogens. Modeled and synthesized a cytokine-based family of compounds that stimulates mucosal immunity.
- Identified likely cytokine molecules and their combinations that result in resistance to pathogens.

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	FY 2006	FY 2007	FY 2008	FY 2009
Noninvasive Biomodulation	2.100	0.000	0.000	0.000

(U) Program Plans:
- Demonstrated new non-invasive approaches to biomodulation.

	FY 2006	FY 2007	FY 2008	FY 2009
Specific Gas Detector	0.500	0.000	0.000	0.000

(U) Program Plans:
- Developed a set of proven, highly sensitive and selective sensors for detecting toxic chemical gases in the HVAC systems of buildings critical to Government operation.

	FY 2006	FY 2007	FY 2008	FY 2009
Novel Sensor for Chemical and BioDefense	1.000	0.000	0.000	0.000

(U) Program Plans:
- Developed novel sensors for chemical and biodefense.

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	FY 2006	FY 2007	FY 2008	FY 2009
Detecting Emerging Classes of Explosives	0.000	1.000	0.000	0.000

(U) Program Plans:
- Explore technologies for emerging classes of explosives.

(U) **Program Change Summary:** *(In Millions)*	**FY 2006**	**FY 2007**	**FY 2008**	**FY 2009**
Previous President's Budget	148.108	112.242	110.695	110.618
Current Budget	132.814	112.814	99.137	106.982
Total Adjustments	-15.294	0.572	-11.558	-3.636
Congressional program reductions	-10.000	-0.428		
Congressional increases	0.000	1.000		
Reprogrammings	-1.500			
SBIR/STTR transfer	-3.794			

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(U) Change Summary Explanation:

FY 2006	The decrease reflects the SBIR/STTR transfer, a $10 million decrease to the Immune Buildings program for the Section 8040 rescission and a $1.5 million below threshold reprogramming.
FY 2007	The increase reflects a congressional add for Detecting Emerging Classes of Explosives offset by a decrease for Section 8106 Economic Assumptions.
FY 2008/09	The decreases reflect program repricing.

(U) Other Program Funding Summary Cost:

- Not Applicable.